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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/733,532	12/11/2003	Julian Edward Sale	18396/2002B	9057

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EXAMINER	
SULLIVAN, DANIEL M	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 11/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/733,532	SALE ET AL.	
	Examiner	Art Unit	
	Daniel M. Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *17-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/11/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This is the First Office Action on the Merits of the application filed 11 December 2003 as a continuation of international application PCT/GB02/02688 filed 11 June 2002, which is a continuation of application 10/146,505 filed 15 May 2002, which is a continuation of application 09/879,813 filed 11 June 2001. The preliminary amendments filed 11 December 2003 and 13 September 2004 have been entered. Claims 1-31, as originally filed, are pending.

Election/Restrictions

Applicant's election of Group I (claims 1-16) in the reply filed on 24 October 2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 17-31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the 24 October reply.

Claims 1-16 are presently under consideration.

Sequence Compliance

In the preexam formalities notice mailed 10 August 2005, Applicant was notified that the application clearly failed to comply with the requirements of 37 CFR. 1.821-1.825 and was required to provide a sequence listing "as well as an amendment directing its entry into the application". The response filed 13 September 2004 does not include a statement directing entry

of the sequence listing into the specification. A response to this Office Action should include a statement referring to the sequence listing filed on 13 September 2004 and directing its entry into the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 and 8-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for preparing a cell line capable of constitutive hypermutation of a target nucleic acid region wherein said cell line is prepared from an B cell, does not reasonably provide enablement for the method wherein the cell used is other than an B cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (a) the nature of the invention; (b) the breadth of the claims; (c) the state of the prior art; (d) the amount of direction provided by the inventor; (e) the existence of working examples; (f) the relative skill of those in the art; (g) whether the quantity of experimentation needed to

make or use the invention based on the content of the disclosure is "undue"; and (h) the level of predictability in the art (MPEP 2164.01 (a)).

Nature of the invention and Breadth of the claims: The instant claims are directed to a method of preparing a cell line wherein a specific region of DNA within the cell is subject to a higher rate of mutation than other DNAs within the cell. As the rejected claims are not limited to practicing the method using any specific starting material, they broadly encompass a method of preparing a cell line capable of directed constitutive hypermutation from any cell.

State of the prior art and level of predictability in the art: The art generally teaches that somatic hypermutation, which provides an increased rate of mutation within defined regions DNA *in vivo*, is a complex and poorly understood process occurring only in B cells. For example, Phung *et al.* (1999) *J. Immunol.* 162:3121-3124 teaches that there are two types of somatic mutation including spontaneous mutation, which is common to all cells and occurs at random throughout the genome, and "hypermutation, which is unique to B cells and is caused by unknown enzymes" (page 3121, left column). Likewise, Papavasiliou *et al.* (2002) *Cell* 109: S35-S44, in an article published at approximately the time the instant application was filed, teaches, "[o]ur understanding of the molecular mechanism of [somatic hypermutation] has been severely limited by the paucity of factors thus far shown to be involved in the reaction" (page S39, left column, second full paragraph). Thus, the art teaches that somatic hypermutation, a process which is required in the instant method, is unique to immunoglobulin-expressing cells (*i.e.*, B cells) and that the cellular machinery underlying the process in B cells was not well understood at the time of filling. Therefore, the skilled artisan would not expect to be able to practice the claimed method for preparing a cell line capable of directed constitutive

hypermutation of a target nucleic acid from any cell other than an immunoglobulin expressing cell without first modifying the cell such that it is capable of somatic hypermutation. As the art provides no guidance as to how one might be able produce a cell capable of somatic hypermutation from a cell that does not ordinarily have that capacity, the skilled artisan must rely on the specification to teach how to practice the full scope of the claimed method without undue experimentation.

Amount of direction provided by the inventor and existence of working examples: The working examples demonstrate two embodiments of the claimed method. In the first, a cell line capable of directed constitutive hypermutation is isolated from an immunoglobulin expressing cell line (i.e., Ramos cell line; Example 4). In this case, a cell population capable of somatic hypermutation was screened to identify spontaneous mutants which had acquired the ability to hypermutate a target sequence without exogenous stimulation. In the second embodiment, the directed constitutive hypermutation rate of an immunoglobulin expressing cell line (i.e., DT40 cells) was enhanced by deletion of the XRCC2 or XRCC3 genes. However, the specification is silent with regard to how one might prepare a cell line capable of directed constitutive hypermutation of a target nucleic acid from a cell line that does not already have the capacity to hypermutate a target nucleic acid.

Relative skill of those in the art and quantity of experimentation needed to make or use the invention: Although the relative level of skill in the art is high, the skilled artisan would not be able to practice the full scope of the claimed method without having to engage in undue experimentation. The art teaches that somatic hypermutation is unique to B cells and that the cellular processes underlying somatic hypermutation remain to be elucidated. Thus, the skilled

artisan would have no idea what method steps would be required to prepare a cell line capable of directed constitutive hypermutation from a cell line that was not already capable of directed hypermutation. Although the teachings of the specification indicate that B cell lines will spontaneously acquire the ability to hypermutate a target sequence in the absence of stimulation, there is no evidence that any cell line other than a B cell line is capable of directed constitutive hypermutation. Further, given the apparent complexity of somatic hypermutation (see Papavasiliou *et al.*), the probability of a cell line spontaneously acquiring the capacity for somatic hypermutation is extremely low. Thus, even if such an event were theoretically possible, the isolation of such a cell would not be routine.

Thus, due to the art recognized unpredictability of acquiring somatic hypermutation in a non-immunoglobulin expressing cell and the lack of guidance in the specification or prior art with regard to how make such a cell, it would require undue experimentation to practice the invention commensurate with the full scope of the claims.

Claims 13-17 are further rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of preparing an immunoglobulin expressing cell line capable of directed constitutive hypermutation of target sequence wherein the rate of mutation in the cell is modulated by administering a mutagen or homozygous deletion of XRCC2 or XRCC3, does not reasonably provide enablement for the method wherein the rate of mutation is modulated by expression of any sequence modifying gene product or any genetic manipulation. The specification does not enable any person skilled in the art to which it pertains,

or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Nature of the invention and Breadth of the claims: As described above, the claims are generally directed to a method of preparing a cell line capable of directed constitutive hypermutation of a target nucleic acid. The method of claims 13-17 further comprise modulating the mutation rate in the cell line by administration of a modifying gene product, by some unspecified genetic manipulation, by manipulation of genes involved in DNA repair or by manipulation of Rad51 analogues or paralogues. The specification does not provide a limiting definition of a sequence modifying gene product and teaches that manipulation includes upregulation, downregulation or deletion. Further, the specification teaches that the cells are genetically manipulated to enhance rates of hypermutation of the Ig V-region (page 15, lines 11-12). Thus, the claims encompass a method of preparing a cell line capable of directed constitutive hypermutation of a target nucleic acid wherein the mutation rate of the cell is modulated by expression of any gene product capable of sequence modification or by upregulation, downregulation or deletion of any gene to enhance the rate of hypermutation of the Ig V-region.

State of the prior art and level of predictability in the art: As discussed above, the art teaches that somatic hypermutation is complex process which remains poorly understood. Thus, the relevant art is undeveloped and unpredictable. Further, the art teaches that the processes of somatic hypermutation are distinct from those of spontaneous mutation (*Id.*). Thus, mutagens or genetic manipulations capable of increasing the rate of spontaneous mutation do not necessarily increase the rate of directed constitutive hypermutation. For example, Sale *et al.* (2001) *Nature*

412:921-926 teaches that ablation of Rad54 and Rad52, which are functionally similar to Rad51, had no effect or reduced the rate of somatic hypermutation in DT40 cells, while ablation of the Rad51 paralogs XRCC2 and XRCC3 apparently resulted in an increased rate of somatic hypermutation (see especially Figure 1 and the caption thereto). It is clear from these teachings that the skilled artisan cannot readily predict which mutagens or genetic manipulations would be useful in a method for preparing a cell line capable of directed constitutive hypermutation of a target nucleic acid and which would actually hinder the process. Thus, the skilled artisan must rely on the instant specification to teach how to practice the claimed method wherein the rate of mutation in the cell is modulated according to the limitations of claims 13-17 without having to engage in undue experimentation.

Amount of direction provided by the inventor and existence of working examples: The teachings of the specification provide no guidance beyond what is available in the art. The disclosure merely states that the method may be practiced with the inclusion of various genetic manipulations (see, e.g., the discussion beginning on page 15, line 9 through the first paragraph on page 16). Other than XRCC2 and XRCC3, the specification provides no guidance that would enable the skilled artisan to identify genetic manipulations that would be useful in the method of preparing a cell line capable of directed constitutive hypermutation of a target nucleic acid.

Relative skill of those in the art and quantity of experimentation needed to make or use the invention: Although the relative level of skill in the art is high, the skilled artisan would not be able to practice the full scope of the claimed invention without having to engage in undue experimentation. The specification and art provide ablation of XRCC2 and XRCC3, two closely related genes, as the only established genetic manipulation useful in the claimed method of

preparing a cell line capable of directed constitutive hypermutation. In spite of this, the general unpredictability of the relevant art and the demonstrated unpredictability of the effect of genetic manipulation of even closely related genes on constitutive hypermutation (*Id.*), the claims encompass the method wherein the rate of mutation in the cell is modulated by expression of any sequence-modifying gene product or by any genetic manipulation. As the one of ordinary skill would have no basis to distinguish those manipulations likely to be useful in the claimed method from those that would not be useful, the skilled artisan would have to resort to empirical experimentation to identify manipulations that could be used in the method. Given the tremendous scope, this would clearly require that the skilled artisan engage in undue experimentation to identify the operative embodiments of the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The claimed method requires selection of a cell in which the rate of target nucleic acid mutation exceeds that of other nucleic acid mutation by a factor of 100, yet the method does not comprise a step wherein the rate of mutation in either the target sequence or other nucleic acid are determined. Further, the claim is indefinite because "other nucleic acid" is not defined in

any meaningful way. The rate of mutation of the "other nucleic acid" is critical to determining whether the cell line meets the limitations of a cell line capable of directed constitutive hypermutation. However, it is reasonable to expect that the rate of mutation is not uniform for all nucleic acids. As the other nucleic acid is not limited to being comprised within the same cell population as the target nucleic acid, an obvious example of this would be another nucleic acid comprised within a cell population having a higher or lower spontaneous mutation rate. Another example would be another nucleic acid comprised within a high copy plasmid vector, which might accumulate mutations at a relatively high rate due to the rapid rate of replication. An additional example would be the mutation rate of a non-functional pseudogene, which would reasonably be expected to have a mutation rate that is higher than that of a gene that is required for cell viability. Still further, if the other gene comprises the required *cis* elements for somatic hypermutation, the mutation rate would be high relative to the mutation rate of other nucleic acids comprised within the genome of the cell. Thus, without some description of the properties of the "other nucleic acid" it is not possible to know what is encompassed by a rate of target nucleic acid mutation that exceeds that of other nucleic acid mutation by a factor of 100 or more.

Claims 2-16 are indefinite insofar as they depend from claim 1.

Claims 2 and 6 are additionally indefinite in the recitation of limitations as derivatives of some starting material. Without a clear statement of the process by which the starting material is derivatized it is not possible to know the metes and bounds of such a limitation because any given starting material can have many divergent derivatives depending on the process of derivatization. Claim 6 is also indefinite in the recitation of "related to" because the claim includes elements not actually disclosed (those encompassed by "related to"), thereby rendering

the scope of the claim unascertainable. In addition, it is not clear from the specification in what way the lymphoid cell line should be related to a type which hypermutates *in vivo.* No guidance is provided as to the properties to be compared and how comparable the properties would have to be to determine infringement issues. Similarly, claim 14 is indefinite in reciting, "one or more genes involved in DNA repair are manipulated". It is unclear from the disclosure what constitutes involvement in DNA repair. For example, must the gene encode a polypeptide that has DNA repair activity, might it encode a regulatory molecule that activates a DNA repair process, or is any gene encoding a polypeptide having an activity related to DNA repair (*e.g.*, synthesis or transport of nucleotides) encompassed by the claim?

Claim 3 is additionally indefinite insofar as it depends from claim 2, claim 7 is additionally indefinite insofar as it depends from claim 6, and claims 15 and 16 are additionally indefinite insofar as they depend from claim 13.

Claim 5 is additionally indefinite in the recitation of "the gene product" in line 1. There is no antecedent basis for "the gene product" in the claims.

Claims 1-7 and 10-13 are additionally indefinite in reciting various properties of "the cell". The antecedent of "the cell" is the product of the process recited in claim 1, which cell is selected from a population. It is not clear whether the limitations recited in the dependent claims are intended to limit the cells of the starting population as well as the isolated cell, or if the limitation only applies to the isolated cell. Thus, the antecedent basis of "the cell" is unclear. Claims 8 and 9 are additionally indefinite insofar as they depend from claim 1.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-13 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 36, 37, 39 and 40 of copending Application No. 10/146,505 in view of Monteiro *et al.* (2000) *Teratogen. Carcinogen. Mutagen.* 20:357-386. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant method is an obvious variation of the claims in the '505 application. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would be obvious over, the reference claim(s).

Claim 1 of the '505 application is directed to a method for preparing a B cell line exhibiting directed constitutive hypermutation of a target nucleic acid region comprising screening B cell lines for ongoing target sequence diversification, wherein said screening comprises determining the mutation rate of the target nucleic acid region relative to the mutation rate of a non-target nucleic acid region, and selecting a B cell line in which the mutation rate of the target nucleic acid region in the selected B cell line exceeds that of the non-target nucleic

acid region in the selected B cell line by a factor of 100 or more, whereby a B cell line exhibiting directed constitutive hypermutation of the target nucleic acid region is prepared.

The instant claims 1-3, 6, 8 and 13 are generic to all that is recited in claim 1 of the '505 application except for the limitation "wherein the rate of mutation in the cell is modulated by genetic manipulation". However, Monteiro *et al.* teaches isolation of cells having desired mutations is enhanced by exposing cells to mutagenic agents. Specifically, Monteiro *et al.* teaches that treatment of cells with mutagenic agents provided a significant increase in the number of cells isolated which exhibited loss of HLA-A2 (see especially the section entitled "Mutation induction experiments" bridging pages 371-372 and Table IV). It would have been obvious to one of ordinary skill in the art seeking to practice the invention claimed in the '505 patent to modify the method to include treating cells with a mutagenic agent—thereby manipulating the genes of the population—according to the limitations of the instant claims. One would be motivated to modify the method claimed in the '505 application according to the teachings of Monteiro *et al.* in view of the nature of the problem solved by the claims of the '505 patent, which is to isolate mutants having a desired property, and in the in order to obtain the expected benefit of a higher mutation rate and therefore an increased incidence of the desired mutation in the cell population. Thus, the instant claims 1-3, 6, 8 and 13, as a whole, would have been obvious over claim 1 of the '505 application in view of the teachings of Monteiro *et al.*

In addition, the limitations of the instant claims 4, 5 and 10 are generic to the limitations recited in claim 40 of the '505 application, the limitations of the instant claim 7 are recited in claim 36 of the '505 application, the limitations of the instant claim 9 are recited in claim 37 of the '505 application, and the limitations of the instant claim 11 are recited in claim 39 of the '505

application. Thus, the instant claims are not patentably distinct from the claims of the '505 application in view of the teachings of Monteiro *et al.* for the reasons set forth herein above regarding the generic claim 1.

This is a provisional obviousness-type double patenting rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Sale *et al.* (April 2000) WO 00/22111 (made of record in the IDS filed 11 December 2003).

Claim 1 of Sale *et al.* (page 41) recites each of the limitations of the instant claim 1 except for the requirement that the rate of mutation in the cell is modulated by a genetic manipulation. Furthermore, claim 2 of Sale *et al.* anticipates the limitations of the instant claims 2 and 3, claim 3 of sale *et al.* anticipates the limitations of the instant claim 6, claim 4 of sale *et al.* anticipates the limitations of the instant claim 7, claim 5 of sale *et al.* anticipates the limitations of the instant claim 8, claim 6 of sale *et al.* anticipates the limitations of the instant claim 9, claim 7 of sale *et al.* anticipates the limitations of the instant claim 10, claim 8 of sale *et al.* anticipates the limitations of the instant claim 11, and claim 9 of sale *et al.* anticipates the limitations of the instant claim 12 except for the requirement that the rate of mutation in the cell is modulated by a genetic manipulation. However, claim 10 of Sale *et al.*, which depends from

each of the preceding claims recites that the rate of mutation in the cell is modulated by the administration of a mutagen, which constitutes genetic manipulation of the cell. Thus, each of claims 1-3 and 6-12 are anticipated by claim 10 of Sale *et al.* as it depends from claims 1-9. Furthermore, the instant claim 13 recites the same limitations as claim 10 of Sale *et al.* and is therefore clearly anticipated thereby. Finally, the instant claims 4 and 5 are directed to the method wherein the cell line expresses the target nucleic acid region in a manner that facilitates selection of cells comprising mutants of said region wherein claim 5 limits the target nucleic acid region to encoding a gene product expressed on the cell surface. These limitations are found, *inter alia*, in the second full paragraph on page 8 of Sale *et al.*, which states, "[w]here the gene product is displayed on the surface of the cell, cells which produce the desired activity may be isolated by detection of the activity on the cell surface, for example by fluorescence, or by immobilizing the cell on a substrate via the surface gene product."

Sale *et al.* teaches a method for preparing a cell line capable of directed constitutive hypermutation comprising each of the limitations of the instant claims. Therefore, the claims are anticipated by Sale *et al.*

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M. Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Friday 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel M Sullivan, Ph.D.
Examiner
Art Unit 1636

11/3/2005

DANIEL M. SULLIVAN
PATENT EXAMINER